

### **REMARKS/ARGUMENTS**

Claims 1-6 are pending in the application and these claims have been rejected. In response, claims 1-2 are canceled from the application without prejudice or disclaimer. Additionally, claim 3 has been amended such that the claim now recites a method of preparing a drug for the treatment of a neurodegenerative phase of multiple sclerosis in mammals, while claim 5 is amended such that the claim now is directed to a pharmaceutical composition for treating a neurodegenerative phase of multiple sclerosis. The proposed claim amendments are completely supported by the application as originally filed (see, e.g., p. 21, lines 17-20) and thus there is no issue of new matter.

Entry of the proposed claim amendments and reconsideration of the application are, therefore, respectfully requested.

#### **Claim Rejection Under 35 U.S.C. §102**

Claims 1-2 are rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Smith, et al., *Veterinary Immunology and Immunopathology*, 78 (2001) pp. 249-262 for the reasons set forth on p. 3.

In response to the rejection, claims 1 and 2 are canceled herein from the application without prejudice or disclaimer. Such cancellation, therefore, renders moot the rejection of the subject claims under 35 U.S.C. §102(b), which should therefore be withdrawn.

#### **Claim Rejection Under 35 U.S.C. §103**

Claims 3-6 are rejected under 35 U.S.C. §103 over the Smith reference (cited above) and further in view of Neely (WO 99/38532) and Jameson et al. (USP 5,589,458) for the reasons set forth at pp. 4-5 of the Office Action. The rejection is respectfully traversed.

In response to the rejection, as indicated above the independent claims 3 and 5 have been amended to limit the use of the drug (claim 3) and the pharmaceutical composition (claim 5) to the treatment of the neurodegenerative phase of multiple sclerosis. Claim 3 as amended thus now recites a method for preparing a drug for the treatment of a neurodegenerative phase of multiple sclerosis in mammals, which method comprises incorporating in said drug a P2X7

purinergic receptor antagonist, wherein the antagonist is selected from the group consisting of Evans Blue, NF279, BBG, o-ATP, KN62, TNP-ATP and HMA. In like manner, claim 5 as presently amended is directed to a pharmaceutical composition for treating a neurodegenerative phase of multiple sclerosis wherein the composition comprises at least one P2X7 purinergic receptor antagonist and at least one pharmaceutically acceptable excipient, wherein the antagonist is selected from the group consisting of Evans Blue, NF279, BBG, o-ATP, KN62, TNP-ATP and HMA.

The Neely reference is directed to a method for inhibiting fibrosis and sclerosis in a subject with a fibrotic or a sclerotic disorder by administering an amount of a P2X antagonist (see, e.g., p. 4, lines 14-17). The reference additionally mentions that sclerosis is a loss of muscular function caused due to an increase in fibrosis.

The Jameson et al. '458 patent discloses that autoimmune diseases are characterized by an immune reaction against one's own antigens. Autoimmune diseases include lupus eritematosus (SLE), rheumatoid arthritis (RA) and Multiple Sclerosis (MS).

The primary Smith et al. reference, in turn, discloses that P2X7 is an ionotropic channel regulated by ATP, playing an important role in a variety of immune responses (p. 249 Introduction and is an important effector pathway of immune response (p. 260, first paragraph). Smith et al. additionally mention that o-ATP and KN62 are antagonists of the purinergic receptors P2X7 (see p. 260, first paragraph).

According to the Office Action the Examiner considers that it would have been obvious, based on the combined teachings of the cited references, for one having an ordinary level of skill in this art to treat an autoimmune disease such as multiple sclerosis (Office Action p. 5). According to the Office Action, a skilled individual would have been motivated to treat an autoimmune disease such as MS since o-ATP is an important immune response effector as disclosed in Smith et al. and the antagonists P2X are useful in the treatment of fibrosis and sclerosis as disclosed by the Neely reference. Furthermore, the Examiner adds in the Office Action that it is known from Jameson et al. that multiple sclerosis is an autoimmune disease.

As indicated above, the scope of the independent claims - and thus all of the remaining claims 3 to 6 - have now been limited to the treatment of the neurodegenerative phase of multiple

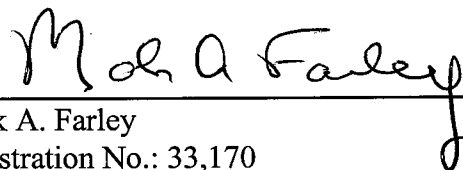
sclerosis. Although the Neely reference discloses that antagonists P2X (not P2X7) are useful in the treatment of sclerosis, Jameson et al. mentions that multiple sclerosis is an autoimmune disease and Smith et al. mentions that P2X7 play an important role in a variety of immune responses and that o-ATP and KN62 are P2X7 antagonists, there is no teaching or suggestion in the cited references, taken in combination, to suggest to one having at least an ordinary level of skill in the relevant art the efficacy of the use of P2X7 in the treatment of the neurodegenerative phase of multiple sclerosis. As taught in the present specification, and as argued (see p. 6) in applicants' prior response dated November 25, 2009, multiple sclerosis is a complex disease which not only has an inflammatory phase, but also a neurodegenerative phase. As a matter of fact, p. 21 lines 17-20 of the present application make it clear that P2X7 can protect against the death of oligodendrocytes and thus they have a protective potential in the neurodegenerative phase of multiple sclerosis.

The above-described capability of P2X7 is not taught or even suggested by any of the cited references, even when combined. Applicants thus respectfully submit that claims 3 and 5 in their amended form would not be obvious to one having an ordinary level of skill in this field of art over the cited combination of references. Furthermore, claims 4 and 6 depend, respectively, upon claims 3 and 5 and include all of the features recited in the subject independent claims. Therefore, dependent claims 4 and 6 are believed to be distinguishable over the combination relied upon by the Examiner to reject the claims for the same reasons as claims 3 and 5. The Examiner is, therefore, respectfully requested to reconsider and withdraw the rejection under 35 U.S.C. 103 of claims 3-6.

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Respectfully submitted,



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